EFFECT OF *THWAY-TOE-KYA-HSEI* (*AHD*-9) COMMONLY USED IN MANDALAY TRADITIONAL MEDICINE TEACHING HOSPITAL ON MODERATE HYPERTENSIVE PATIENTS

Ei Ei Cho[1], Aye Chan Thu Zar Hlaing[1], Win Myint[1], Win Naing[1], Kyi Kyi Oo[2], Theim Kyaw[1], Kyaw Oo[2]

INTRODUCTION

- Hypertension is the most common cardiovascular illness and is a major public health issue in developed as well as in developing countries
- In more than 95% of cases, a specific underlying cause of hypertension cannot be found and such patients are said to have primary or essential hypertension

- The pathogenesis of H/T includes many factors, such as renal dysfunction, autonomic tone, insulin resistance and neurohumoral factors, high salt intake, heavy consumption of alcohol, obesity, lack of exercise, impaired intrauterine growth and stress
- H/T is the most important risk factor for myocardial infarction (MI), heart failure and stroke in older people

Definition of Hypertension (WHO)

- systolic blood pressure of 160 mmHg or more and / or a diastolic blood pressure of 95 mmHg or more

Classification of Hypertension

Hypertension	Systolic BP (mmHg)	Diastolic BP (mmHg)
Grade 1 Hypertension (mild)	140-159	90-99
Grade 2 Hypertension (moderate)	160-179	100-109
Grade 3 Hypertension (severe)	≥180	>110

According to the concepts of *Desana* medicine

- Hypertension is a disease of ***Saṅgahita*** in Eight disease patterns
- Causative factors of *Saṅgahita* are *Sīta Tejo*, excess of internal *Pathavī* and predominance of external *Āpoābadana*
- it is diagnosed as *Sīta pathavī ābadana*

- Globally cardiovascular disease accounts for approximately 17 million deaths a year
- Complications of hypertension account for 9.4 million deaths worldwide every year
- Hypertension is responsible for at least 45% of deaths due to heart disease and 51% of deaths due to stroke (WHO, 2013)

Prevalence of hypertension is increasing in many countries in the Region :

- In India, raised BP increased → 5% - 12% in 1960 to 1990 and more than 30% in 2008
- In Indonesia, raised BP increased → 8% in 1995 to 32% in 2008
- In Myanmar, increase in high BP prevalence → 18% - 31% males, and16% - 29% females during 2004–2009

- According to the data of Traditional Medicine Teaching Hospital (TMTH), Mandalay in 2013-2014, hypertension was the 4th common health problems out of ten
- In 2015, about 1516 (5.9) % cases were hypertensive patients in TMTH, Mandalay

In Traditional Medicine, varieties of **Myanmar traditional antihypertensive drugs** such as :

- *Thway-Hsei-Ni-Gyi*
- *Zar-Ti-La-Wun-Ga*
- *Pyi-Lone-Chan-Tha*
- *Hsei-Pale-Kalart*, etc

- *AHD*-9 has been used in Mandalay Traditional Medicine Teaching Hospital by traditional medicine practitioners based on their experience since 2006
- commonly used in Medical ward, Physical Medicine ward and Gynecological ward, TMTH, Mandalay
- *AHD*-9 is composed of nine plant materials and formulated by equal amount of plant ingredients

- These plant materials are used in hypertension, cardiac tonic, paralysis, hemiplegia, indigestion, arthritis, diabetes mellitus and dysentery etc
- Predominant tastes of *AHD*-9 are hot, bitter and pungent and according to *Desana* Medicine Concept, these tastes are effective for *Saṅgahita* diseases

- Aye-Chan-Thu-Zar-Hlaing (2015) investigated the acute and sub-acute toxicity of *AHD*-9 in rats and was non-toxic effects
- *AHD*-9 has not scientifically been experimented as clinical trial yet
- Therefore, this study aimed to find out the effect of *AHD*-9 on hypertensive patients

- Win Naing (2012) studied antihypertensive effect of Modified *TMF*-28 in uncomplicated hypertensive patients and the result was highly significant
- Modified *TMF*-28 was selected as the control drug to compare the effectiveness of *AHD*-9 in this study

OBJECTIVES

General Objective

- To study the effect of *Thway-Toe-Kya-Hsei (AHD*-9) used in Mandalay Traditional Medicine Teaching Hospital on moderate hypertensive patients

Specific Objectives

(1) To determine the blood pressure of moderate hypertensive patients before treatment (day 0)

(2) To determine the blood pressure of moderate hypertensive patients on the *AHD*-9 during treatment (day 1, day 2 and day 3) and after treatment (day 4)

(3) To compare the effect of the *AHD*-9 on day 0 (before treatment) and day 1, day 2, day 3 (during treatment), day 4 (after treatment)

(4) To determine the blood pressure of moderate hypertensive patients on the modified *TMF*-28 during treatment (day 1, day 2 and day 3) and after treatment (day 4)

(5) To compare the antihypertensive effects of the *AHD*-9 and the modified *TMF*-28 on day 0 (before treatment), day 1, day 2, day 3 (during treatment) and day 4 (after treatment)

METHODOLOGY

Study Design

Randomized controlled trial

Study Site

Kyaung Htai Monastery Training School, State *Pariyatti Sasana* University, *Shwe Si Sasana* Monastery and *Alinkar Yarma Shwe Bo* Monastery from *Aung Myay Thar San* Townships, Mandalay Region

Study Period

The study was done from 1st August 2016 to 31st July 2017

Study Population

Known cases of moderate hypertensive patients who fulfilled the inclusion criteria from *Kyaung Htai* Monastery Training School, State *Pariyatti Sasana* University, *Shwe Si Sasana* Meditation center and *Alinkar Yarma Shwe Bo* Monastery at *Aung Myae Thar San* Township, Mandalay

Sampling Method

Blinding block randomization method

Selection Criteria

Inclusion criteria

1) Age - 35 to 65 years old
2) Sex - both sexes
3) Known cases of Grade 2 Hypertension (Moderate hypertensive patients) - BP: 160/100 mmHg to 179/109 mmHg without any medication for at least 72 hours

Exclusion criteria

1) The patients who had been taking any anti-hypertensive drug within 72 hours.
2) The patients with severe hypertension (BP: 180/110 mmHg and above)
3) Patient with known cases of diabetes
4) Pregnant woman and lactating mother
5) Chronic alcohol drinker

Materials

- Mercury sphygmomanometer with cuff size 12×22 cm (MAC mercurial sphygmomanometer, model 300, Matsuoka Meditech corp; Japan)
- Stethoscope (MAC Stethoscope, Matsuoka Meditech corp; Japan)
- *Thway-Toe-Kya-Hsei* (*AHD*-9)
- *MTMF*-28

No.	Myanmar Name	Scientific Name	Part used	Weight			Percentage
				Myanmar Unit		Metric Unit	
				Kyat	Pe	Gram	
1.	Kyat-Thun- Phyu	*Allium sativum* L.	Bulb	10 k	-	160 g	11.11 %
2.	Sin-Tone-Ma Nwe	*Tinospora cordifolia* Miers.	Stem	10 k	-	160 g	11.11 %
3.	Saung-May Khar	*Picrorrhiza kurroa* Royle.	Root	10 k	-	160 g	11.11%
4.	Nanwin- Khar	*Curcuma comosa* Roxb.	Rhizome	10 k	-	160 g	11.11 %
5.	Nant-Thar-Phyu	*Santalum album* L.	Wood	10 k	-	160 g	11.11%
6.	Nant-Thar-Ni	*Pterocarpus santalinus* L.	Wood	10 k	-	160 g	11.11 %
7.	Bohnma-Yarzar	*Rauwolfia serpentina* L.	Root	10 k	-	160 g	11.11%
8.	Thana-Khar	*Hesperethusa carenulata* Roxb	Root	10 k	-	160 g	11.11%
9.	Aykayit	*Millingtonia hortensis* Linn.	Root	10 k	-	160 g	11.11%
Total weight				90 k	-	1440g	100 %

No.	Myanmar Name	Scientific Name	Part used	Amount in g/100g
1	Thetyinngyee	*Croton oblongifolius*	Root	50.0
2	Hsoogauknet	*Capparis sepiaria*	Bark	5.6
3	Kadet	*Crataeva religiosa* Forst.	Bark	5.6
4	Ngayoke Kaung	*Piper nigrum*	Fruit	5.6
5	Zaunggyan	*Osyris Wightiana*	Fruit	5.6
6	Peik chinn	*Piper longum*	Fruit	5.6
7	Awle	*Sapium sp.*	Stem	5.6
8	Gyin	*Zingiber officinale*	Rhizome	5.6
9	Hsaypale	Gentiana kurroo	Root	5.6
10	Kantkalar	*Gisekia pharnaceoides* Linn.	The whole plant	5.6
Total weight				100.4

Tinospora cordifolia **Miers.**

Curcuma comosa **Roxb.**

Pterocarpus santalinus **L.**

Millingtonia hortensis Linn.

Santalum album L.

Picrorrhiza kurroa Royle.

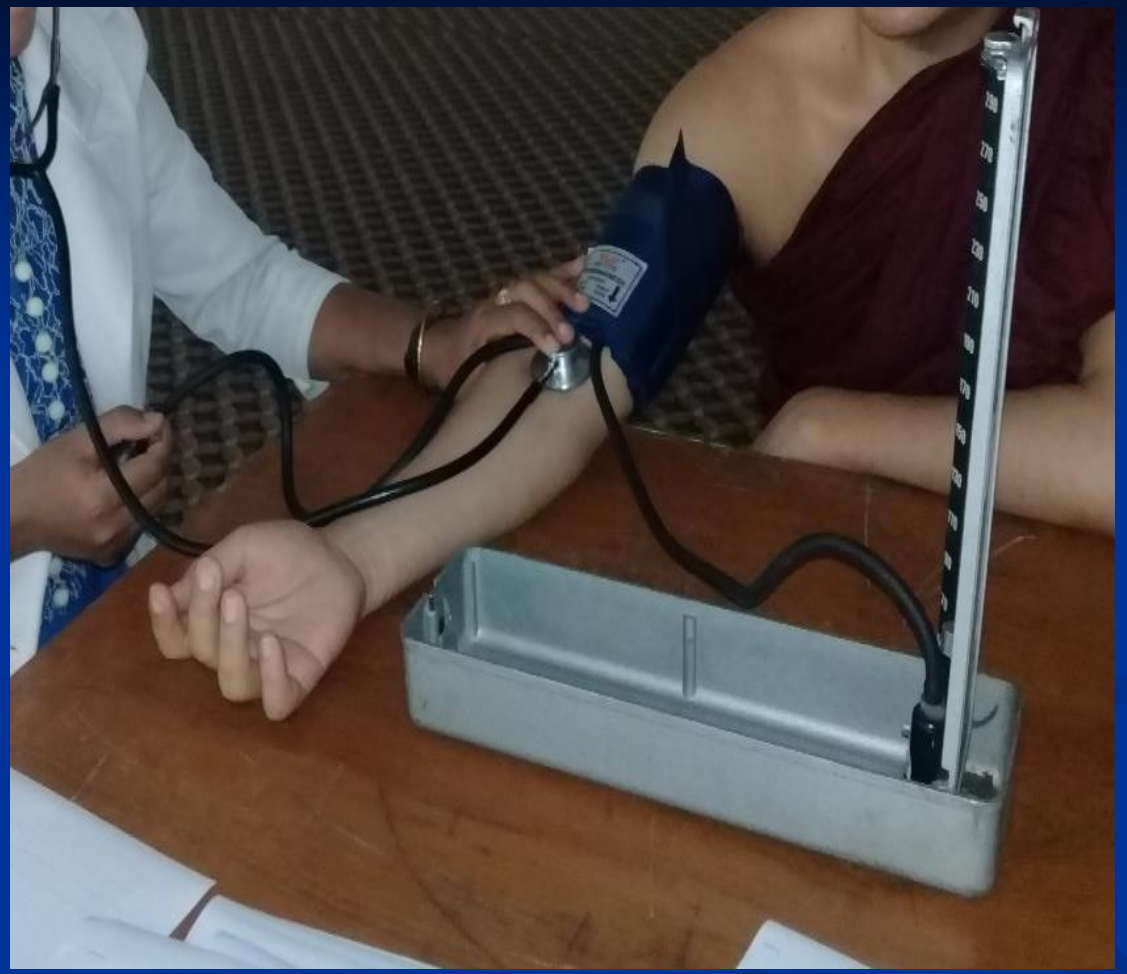
Rauwolfia serpentina L.

Allium sativum L.

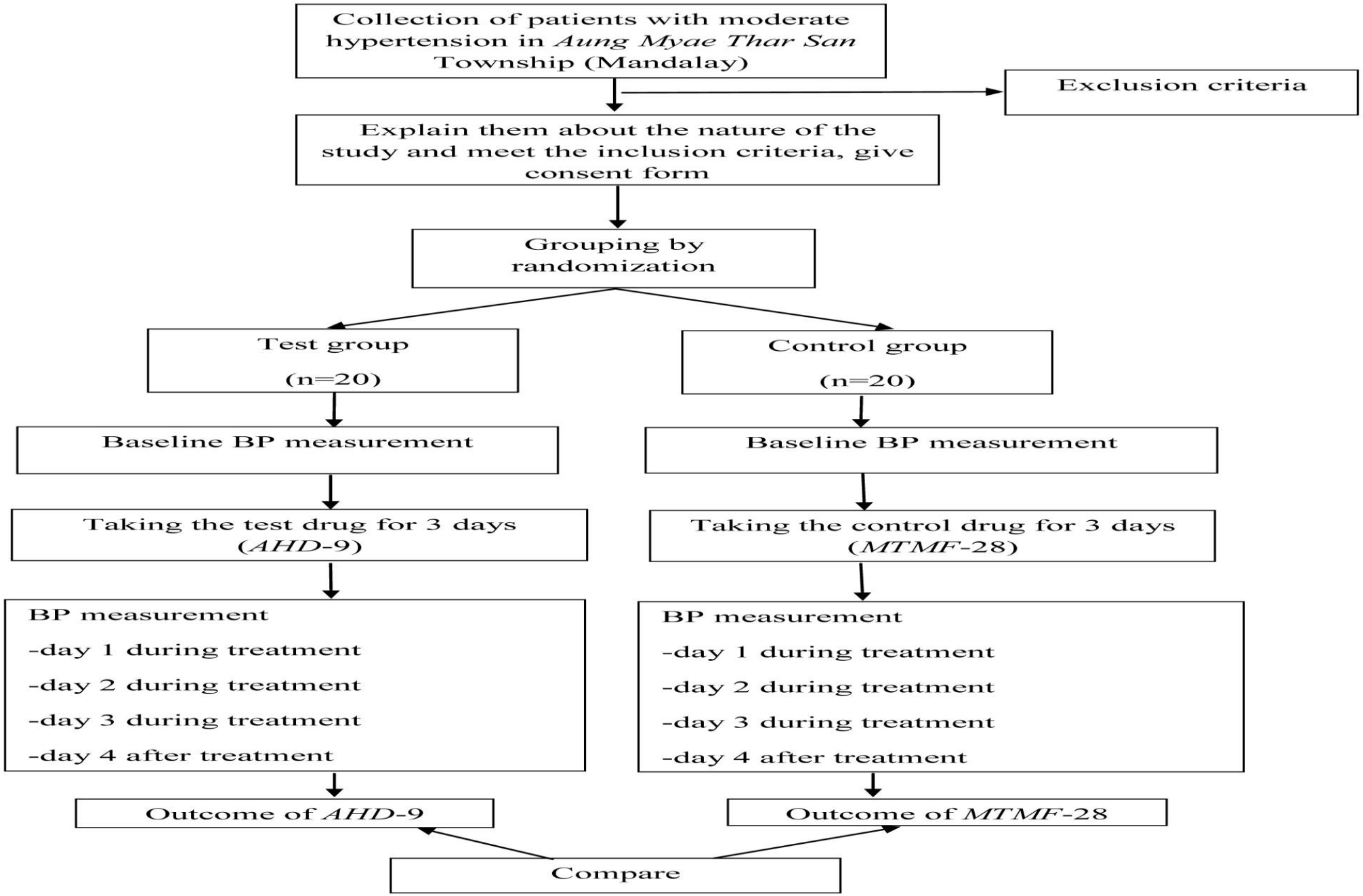
Hesperethusa carenulata **Roxb**

Modified TMF- 28

AHD - 9



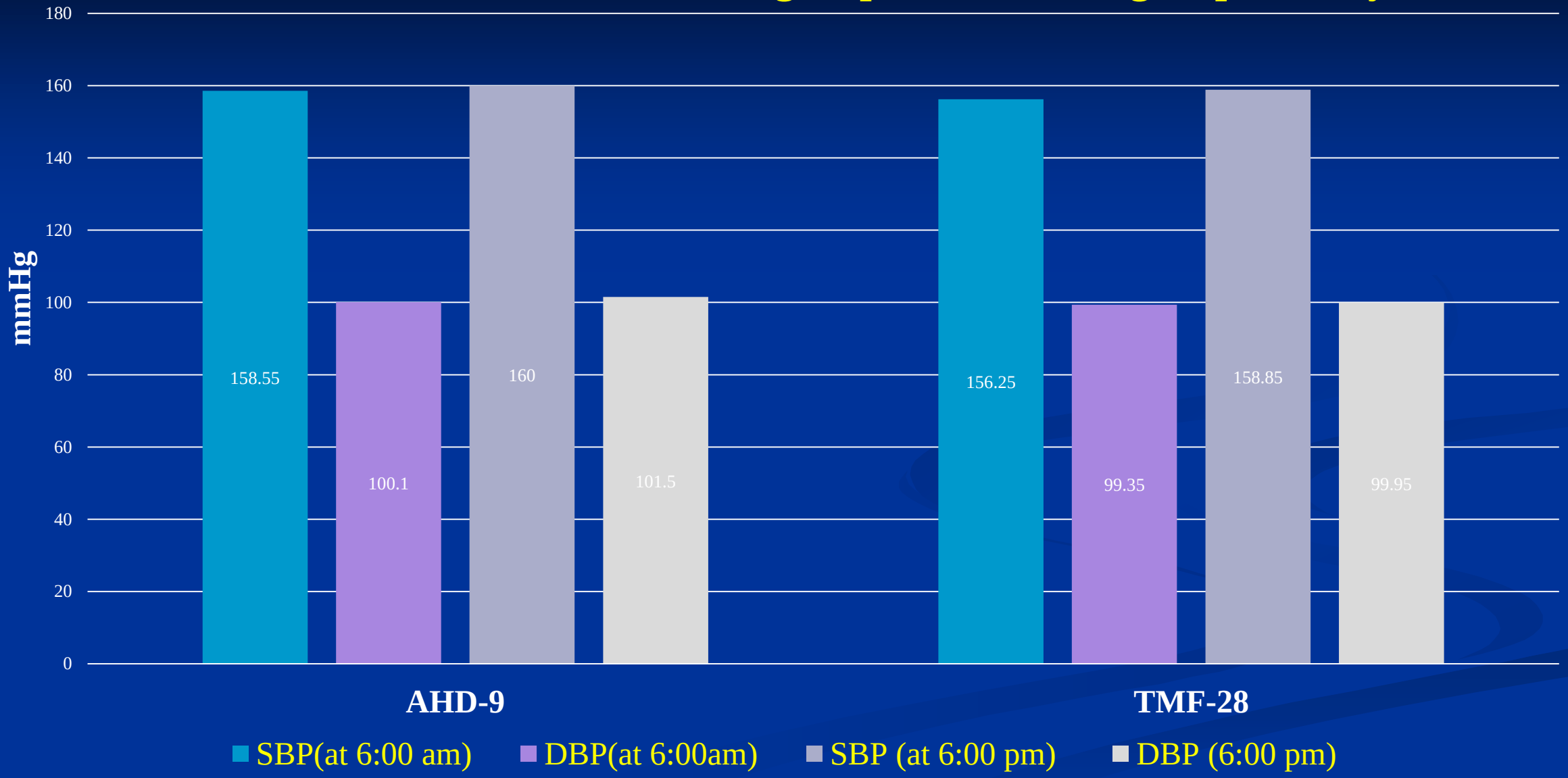
Measurement of the blood pressure of hypertensive patient



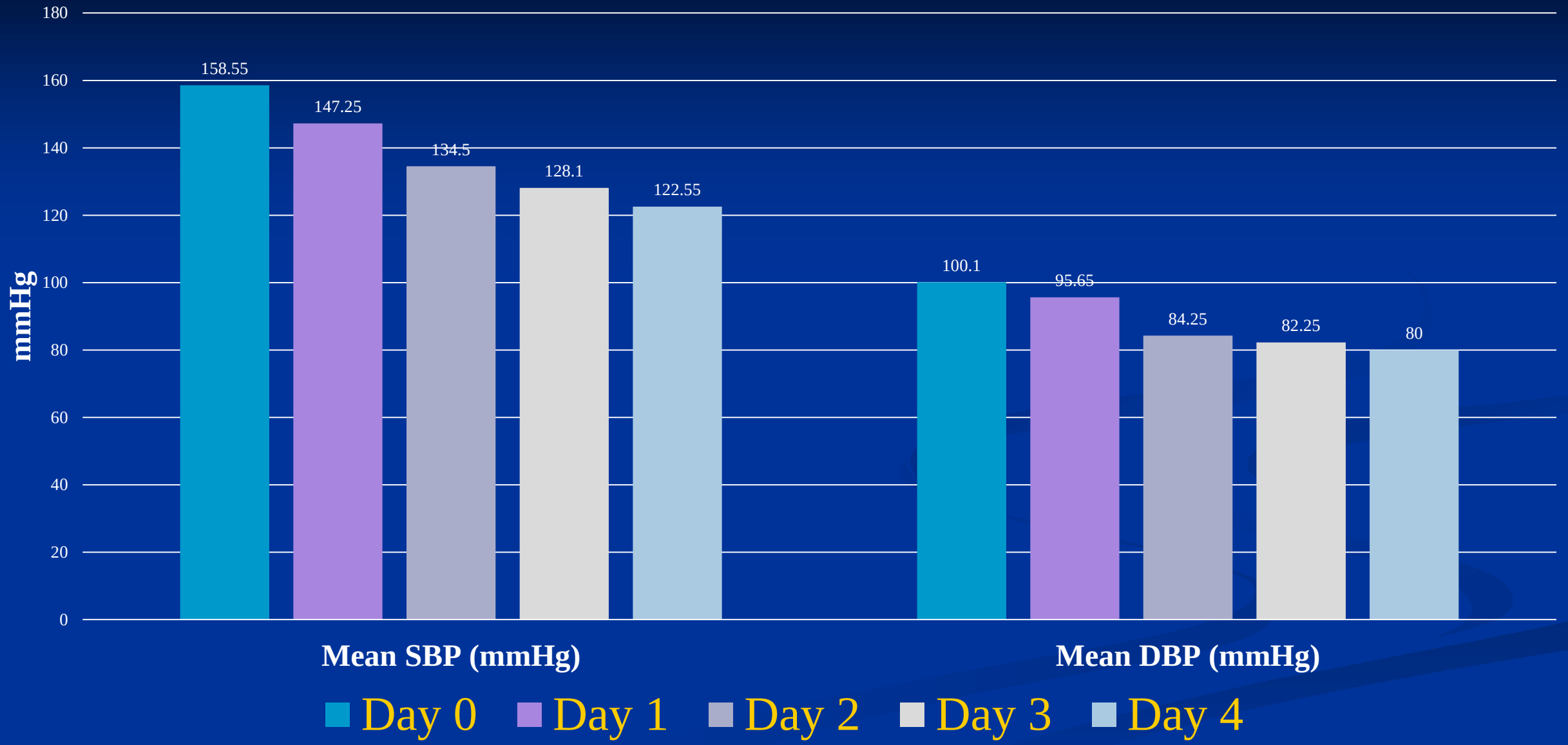
Flow chart of study procedure

RESULTS AND DISCUSSION

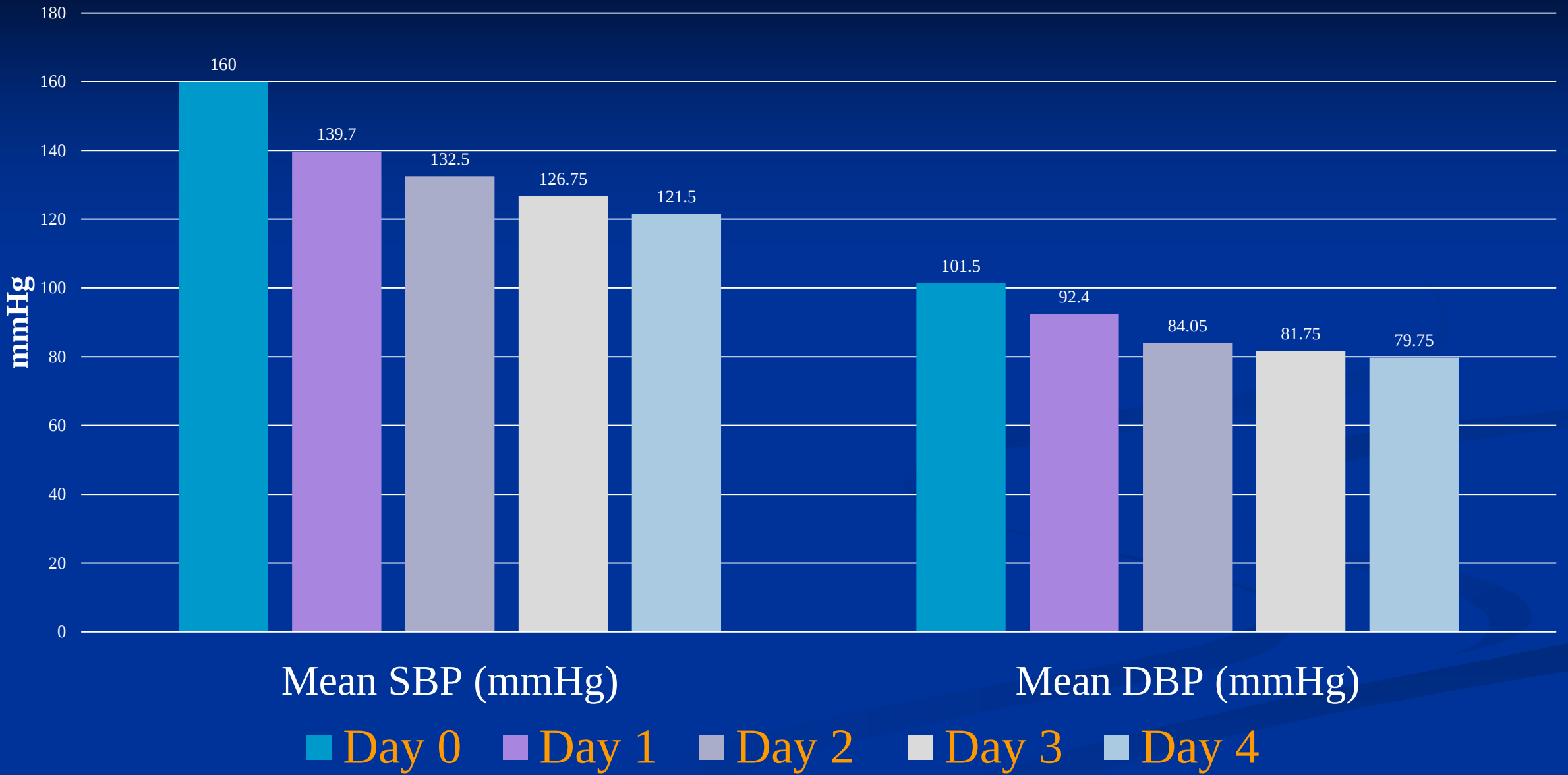
Mean Blood Pressure in the Test group and Control group for Day 0



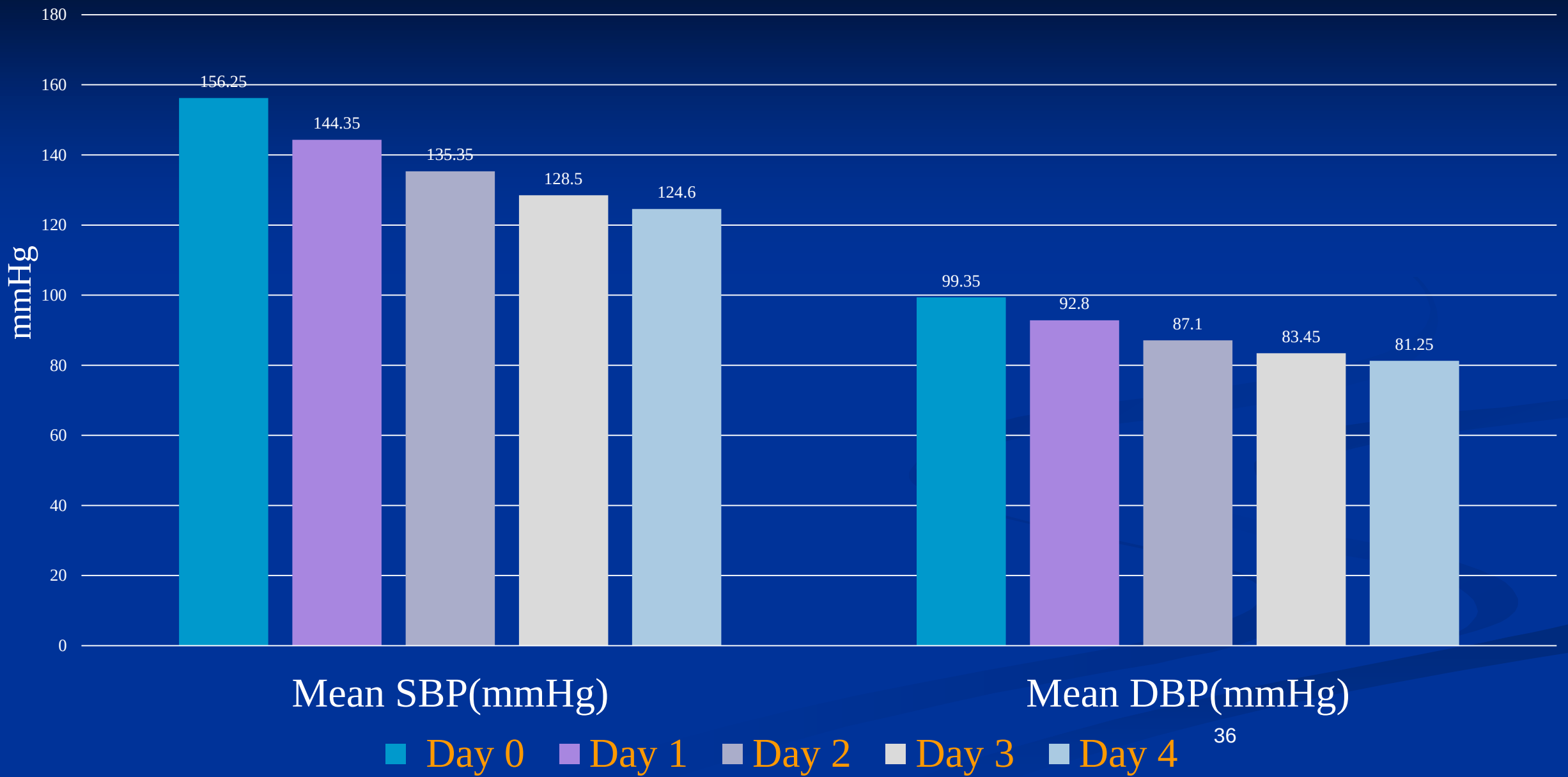
AHD-9 at 6:00 am



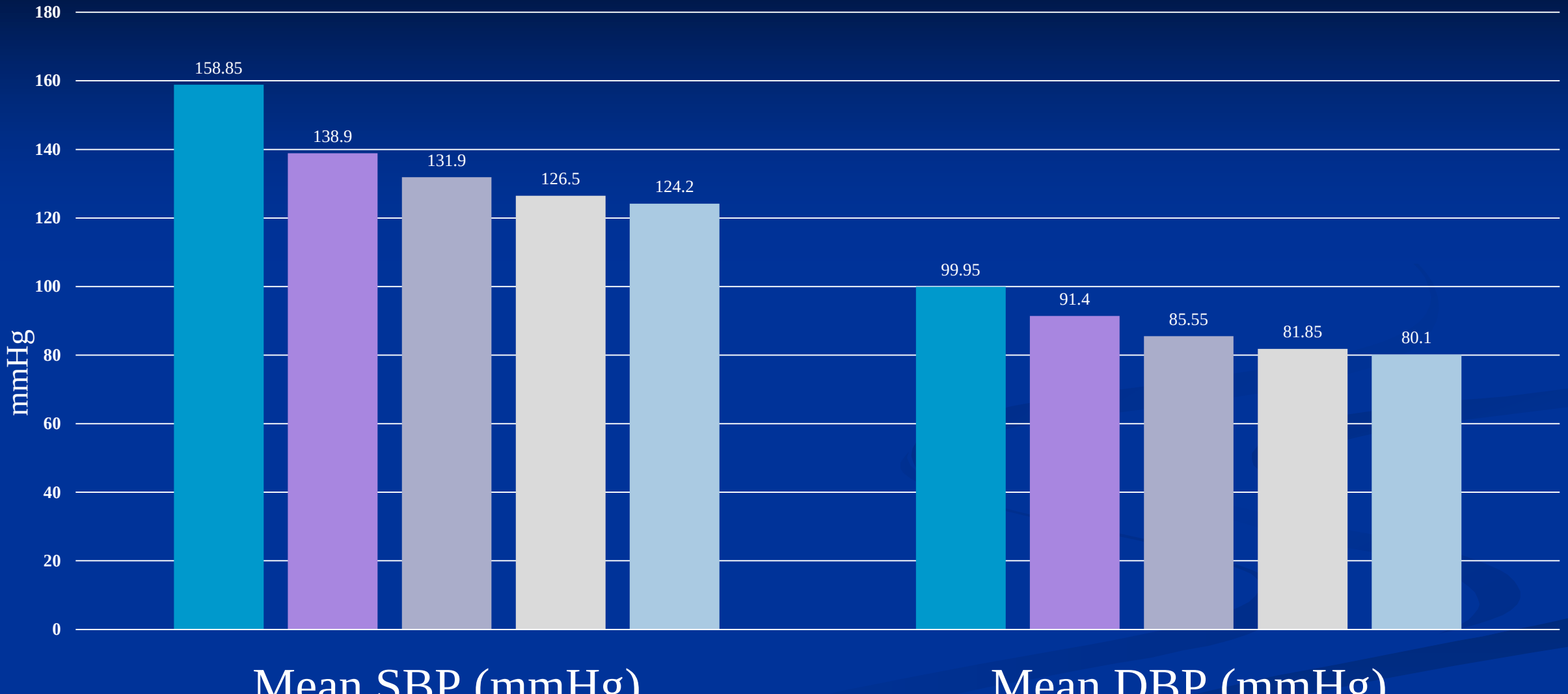
AHD-9 at 6:00 pm



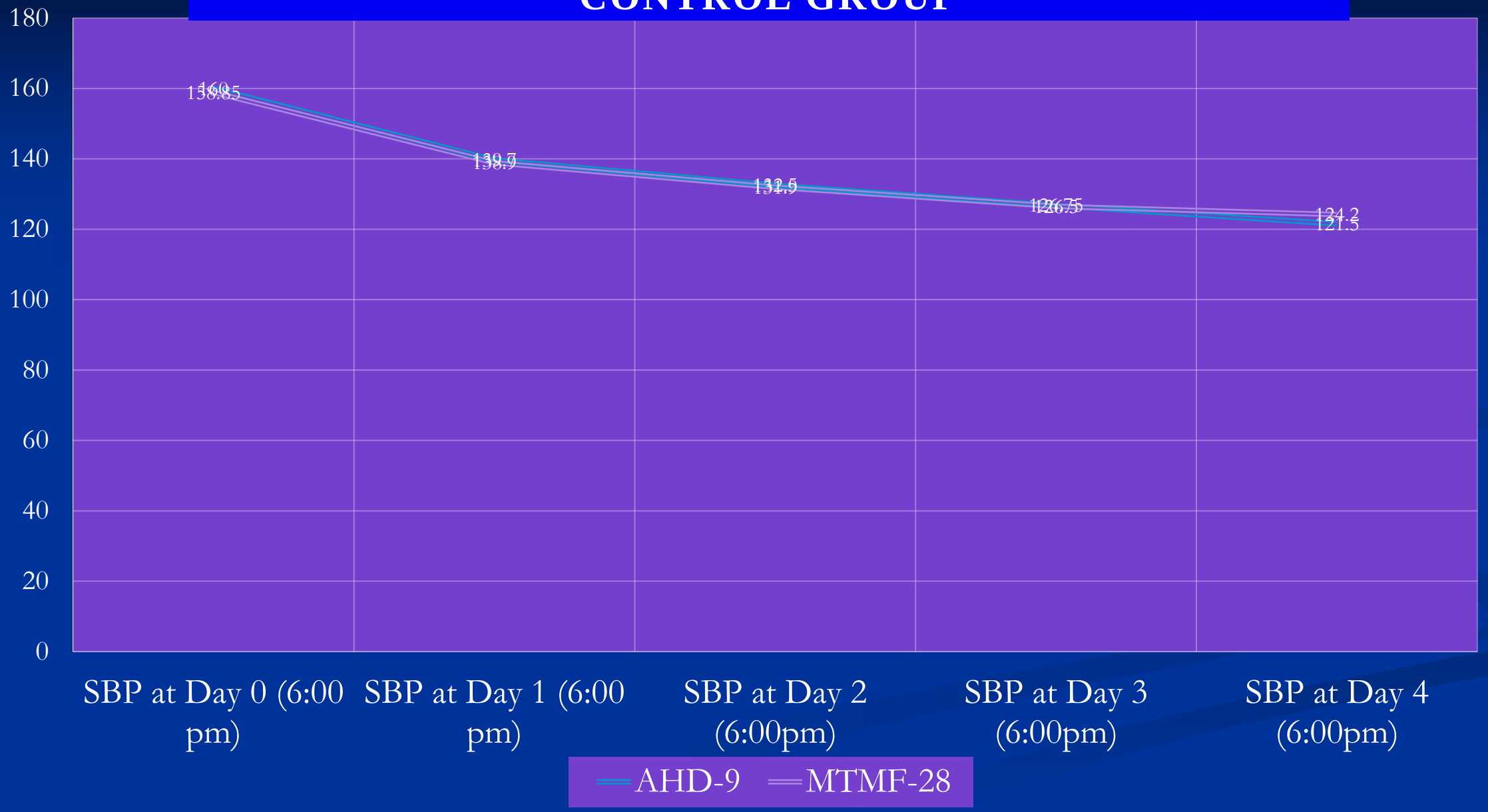
MTMF-28 at 6:00 am



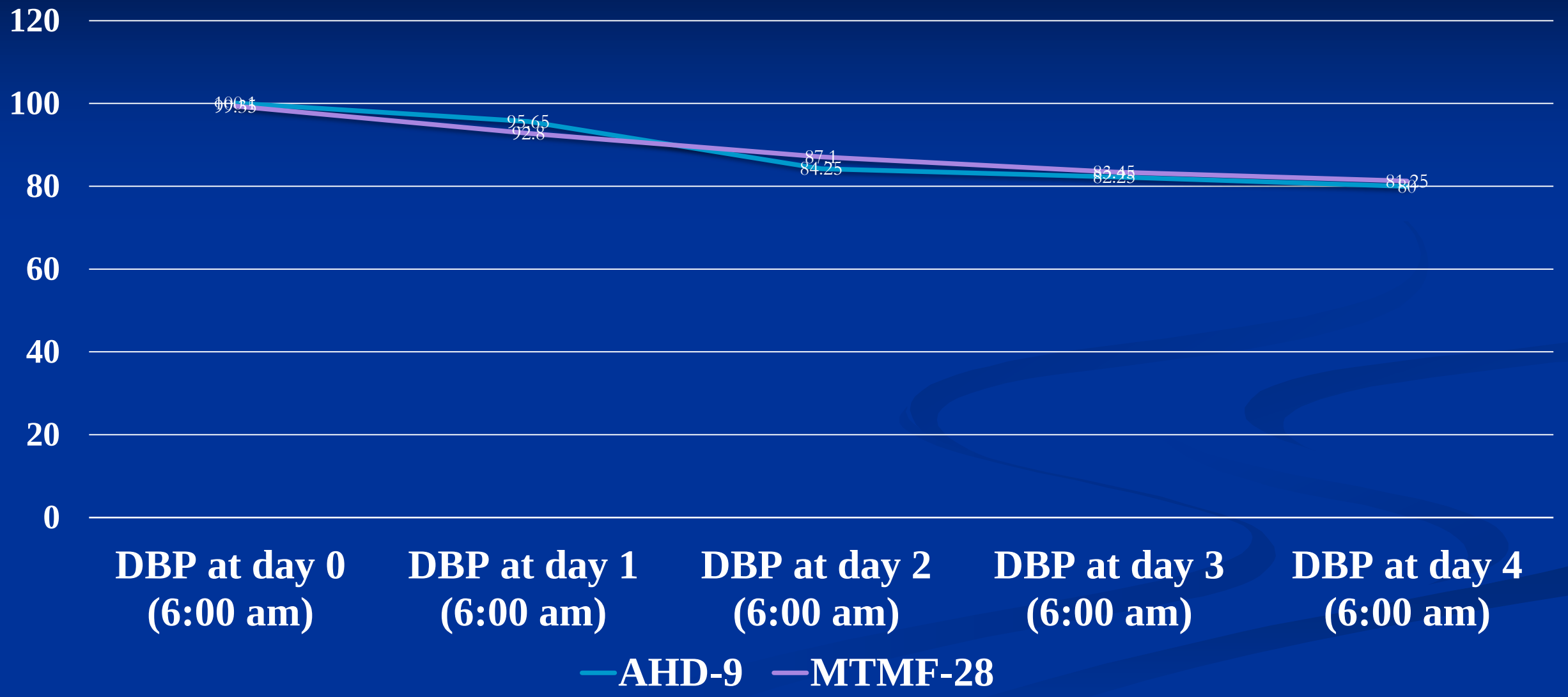
MTMF- 28 at 6:00 pm



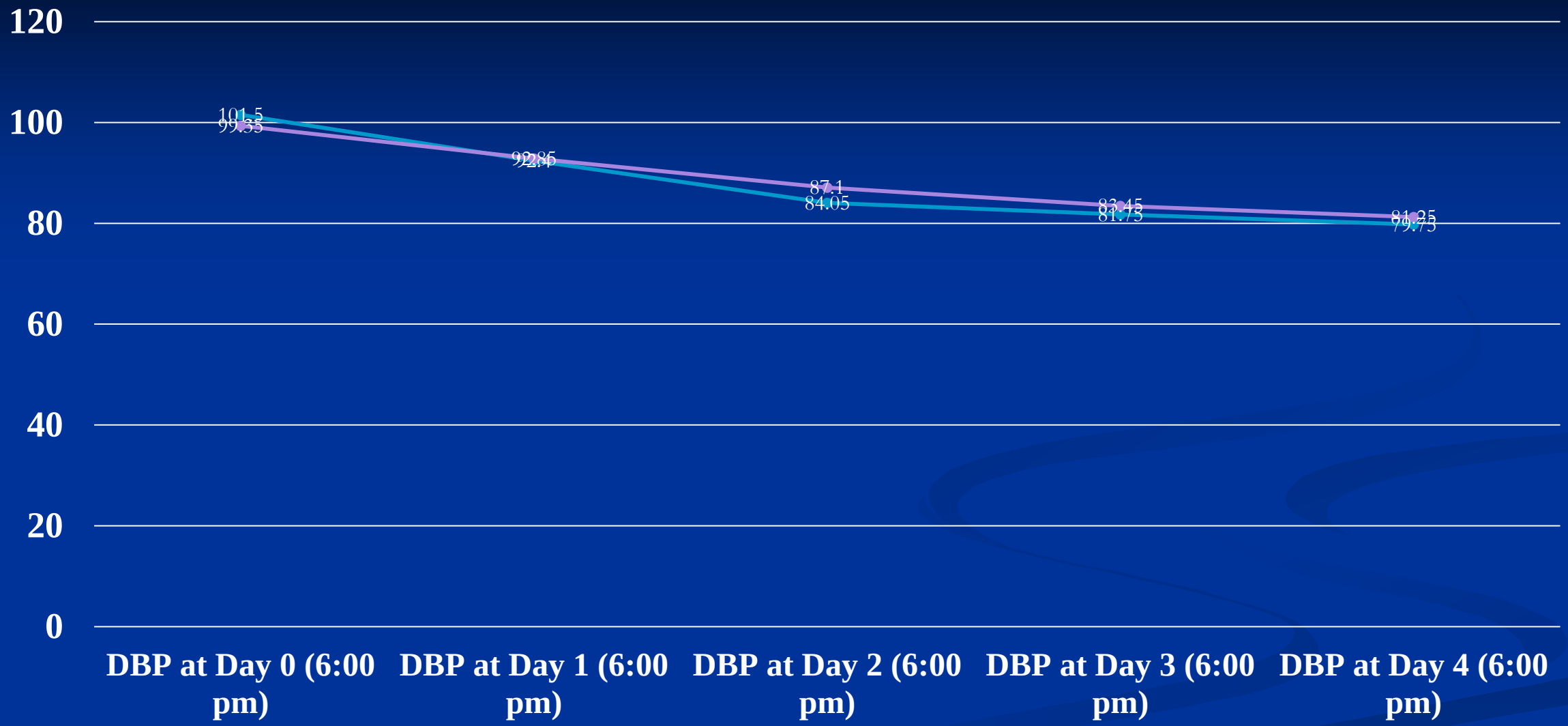
COMPARISON OF MEAN SBP IN THE TEST GROUP AND CONTROL GROUP



Comparison of Mean DBP in the Test group and Control group



Comparison of Mean DBP in the Test group and Control group



	Time	BP	Day 0	Day 4	Std. Deviation	Mean Difference	*t*	df	p-value
***AHD*-9**	6:00 am	SBP	158.55	122.55	8.11756	36.0	19.833	19	0.000
		DBP	100.10	80.00	7.62199	20.10	11.793	19	0.000
	6:00 pm	SBP	160.00	121.50	6.90156	38.50	24.948	19	0.000
		DBP	101.50	79.75	7.30447	21.75	13.316	19	0.000
***MTMF* 28**	6:00 am	SBP	156.25	124.60	7.79524	31.6	18.158	19	0.000
		DBP	99.35	81.25	8.23280	18.10	9.832	19	0.000
	6:00 pm	SBP	158.85	124.20	9.34866	34.65	16.576	19	0.000
		DBP	99.95	80.10	7.85577	19.85	11.300	19	0.000

- *AHD*-9 was effective in lowering high SBP and DBP
- SBP and DBP of patients were significantly reduced in both test group and control group
- Not only significant changes in heart rate but also obvious side effects were not found

- In comparison of blood pressure between *AHD*-9 and *MTMF*-28, it was found that there was approximately similar reduced the blood pressure of moderate hypertensive patients
- Therefore, it was clinically antihypertensive effect of *AHD*-9 commonly used in TMTH on moderate hypertension

CONCLUSION

- *AHD*-9 had significant blood lowering effect in all age groups of both sexes for the treatment of moderate hypertension
- Obvious side effects and special complaints of the subjects were not reported during study

- At 6:00 am, *AHD*-9 decreased Mean SBP and DBP from the base line level (before treatment) by 36 mmHg and 20 mmHg (day 4- at the end of treatment) respectively
- At 6:00 pm, *AHD*-9 decreased Mean SBP and DBP from the base line level (before treatment) by 38.5 mmHg and 21.75 mmHg (day 4- at the end of treatment) respectively

- Therefore, it can be determined that the test drug (*AHD*-9) has the lowering effect of the blood pressure
- The results of this study would be useful as a treatment guide and rational prescription of drug for the management of hypertension

RECOMMENDATIONS

According to the results of this study,

- present study was carried out with limited sample size and also for short term
- further study should be carried out with large sample size for appropriate time

- effect on pregnancy and lactating mother were not known and further study will be necessary to be conducted
- effect of *AHD*-9 was studied only on the monks, nuns and yogis
- should be studied other moderate hypertensive patients except monks, nuns and yogis

REFERENCES

- တိုင်းရင်းဆေးပညာဦးစီးဌာန (၁၉၉၀) ၊ တိုင်းရင်းဆေးပညာဦးစီးဌာနသုံးဆေးနည်းများ။
- နာဂသိန် (အရှင်) (၁၉၇၆)၊ ပုံပြဆေးအဘိဓာန်၊ ပထမတွဲ၊ ဟံသာဝတီပိဋကတ်ပုံနှိပ်တိုက်. ရန်ကုန်၊ မြန်မာ
- နာဂသိန် (အရှင်)၊ (၁၃၃၂)၊ နာဠီပရိကွယာမူရင်းကျမ်း၊ မဂ်လာပုံနှိပ်တိုက်၊ ဒုတိယအကြိမ်၊ ရန်ကုန်
- ဝင်းမြင့် (ဦး)၊ သန်းထွန်း (ဦး) နှင့် မောင်မောင်သက် (ဦး)၊ (၂၀၀၆)၊ ရောဂါကြီး (၆) မျိုးအား တိုင်းရင်းဆေးပညာနည်းစနစ်ဖြင့် လေ့လာခြင်း၊ မြန်မာ့တိုင်းရင်းဆေးပညာဘွဲ့စာတမ်း၊ တိုင်းရင်းဆေးတက္ကသိုလ်၊ မန္တလေး၁၃၊၁၄၊၁၅၊၁၈၊၁၉။

- Amornnopparattanakul P., NantakaKhorana N., and Viyoch J. (2012). Effects of *Hesperethusa Crenulata*'s Bark Extract on Production of Pro-Collagen Type I and Inhibition of MMP-1 in Fibroblasts Irradiated UVB International Conference on Biological, Biomedical and Pharmaceutical Sciences, Pattaya Thailand.
- Aye-Chan-Thu-Zar-Hlaing (2015). Acute and Subacute Toxicity study of *Thway-Toe Kya-Hsei* of Traditional Medicine Teaching Hospital in Rat, MMTM Dissertation, UTM, Mandalay.

- Deshmukh S. R., Ashrit D. S. and Patil B. A. (2012). Extraction And Evaluation Of Indole Alkaloids From *Rauwolfia Serpentina* For Their Antimicrobial And Antiproliferative Activities, International Journal of Pharmacy and Pharmaceutical Sciences, Department of Biotechnology, New Arts, Commerce and Science College, Ahmednagar, Vol 4. India.

- European Society of Hypertension (ESH), 2003, European Society of Cardiology (ESC), Guidelines committee. guidelines for the management of arterial hypertension. *Journal of Hypertension*. 21;1011-1053.
- Heart foundation. (2016). Guideline for the diagnosis and management of hypertension in adults.
- Khare C.P. (2007). Indian medicinal plants. An Illustrated dictionary. New Delhi, India.

- Khine-Khine-Lwin, Mu-Mu-Sein-Myint, May-Aye-Than, Min-Min-Myint-Thu Thaung-Hla, Khin-Tar-Yar-Myint, Aung-Myint and Ei-Ei-Soe. (2011). Acute and Sub-acute toxicity of *Millingtonia hortensis* Linn. f. (*Aykayit*) leaves in animal model.
- Min-Han. 2007, Clinical trial of the effect of *plantago major* Linn on the treatment of uncomplicated hypertension. (Ph.D.Thesis), University of Medicine, Mandalay

- Newby, D.E., Grubb, N.R., Bradbury, A., (2014). Walker, B.R., Colledge, N.R., Ralston, S.H. and Penman, I.D. Davison's Principles & Practice of Medicine. 22nd Edition, Volume 2, Churchill Livingstone Elsevier. 607.
- Rathod, M.R. and Kumar, S.A., (2012).Understanding of Hypertension in *Ayurveda*.Scientific report; 2-3
- Sanapeti R.V and Chaganti S. (2012). Etiopathogenisis of hypertension in Ayurveda. Int. J. Res. Ayurveda. Pharm; 3 (6):787-788.

- Sindhu R. K., Kumar U. A. and Arora S. (2010). *Santalum album* L.:A Review On Morphology, Phytochemistry And Pharmacological Aspects, International Journal of Pharm Tech Research, Vol.2, No.1
- Win-Myint. (2012). A Study on Combined Effects of *TMF*-27 and *TMF*-35 on Patients with Type 2 Diabetes Mellitus, MMTM Dissertation, University of Traditional Medicine, Mandalay

- Win-Naing (2012). Study on Antihypertensive Effect of Modified *TMF*-28 in Uncomplicated Hypertensive patients, MMTM, Dissertation, University of Traditional Medicine, Mandalay
- WHO. (2013). A global brief on hypertension, Silent killer, Global public health crisis. 17-2.

ACKNOWLEDGEMENT

- Director General, Department of Traditional Medicine
- Rector, University of Traditional Medicine, Mandalay and all members of the Protocol Board of Studies
- Head of DOM, senior and junior colleagues from Department of Medicine and University of Traditional Medicine

- Dr. Kyaw Oo, Deputy Director General, Department of Health Professional Resource Development and Management, Nay Pyi Taw for his kind help in statistical analysis on my data
- Thank to Professor Dr. San San Htay, Professor/Head and Dr. Su Ye Toe, Assistant Lecturer, Preventive and Social Medicine Department, University of Medicine, Mandalay for their helping in sample size calculation

- all Buddhist monks, nuns and yogis living in *Kyaung Htai* monastery Training School, State *Pariyatti Sasana* University and *Shwe Si* Medication center
- all the persons who helped us directly or indirectly throughout our carrier

THANKS FOR ATTENTION!